

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Hermann Bujard, and  
Manfred Gossen

Serial No.: N/A

Filed: September 29, 1998  
(Continuation of Serial No. 08/479,306)

For: *TETRACYCLINE-REGULATED  
TRANSCRIPTIONAL ACTIVATOR FUSION  
PROTEINS (as amended)*

Attorney Docket No.: BBI-013C3CN

Group Art Unit:

Examiner:

COPY

Box Patent Application  
Assistant Commissioner for Patents  
Washington, D.C. 20231

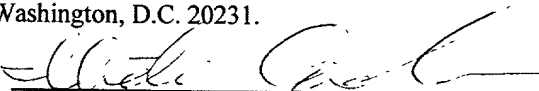
CERTIFICATION UNDER 37 CFR 1.10

Date of Deposit: September 29, 1998

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I hereby certify that this 37 CFR 1.53(b) request and the documents referred to as attached therein are being deposited with the United States Postal Service on the date indicated above in an envelope as "Express Mail Post Office to Addressee" service under 37 CFR 1.10 and addressed to the Assistant Commissioner for Patents, Box Patent Application, Washington, D.C. 20231.

Ilidio P. Cardoso  
Name of Person Mailing Paper

  
Signature of Person Mailing Paper

PRELIMINARY AMENDMENT

Dear Sir:

Prior to examination of the above-identified application, please amend the application as follows:

In the Specification:

At page 1, line 3, please delete the original title and insert the following new title:  
--Tetracycline-Regulated Transcriptional Activator Fusion Proteins--.

At page 1, line 6, under the heading "Related Applications", please delete lines 6-9, and insert the following:

--This application is a continuation of U.S. Serial No. 08/479,306, filed June 7, 1995, pending, which is a continuation-in-part of U.S. Serial No. 08/260,452, filed June 14, 1994, now U.S. Patent No. 5,650,298, which is a continuation-in-part of U.S. Serial No. 08/076,327, filed June 14, 1993, now abandoned. The entire contents of each of these applications are incorporated herein by reference.--

At page 6, line 12, please delete "Fig. 1 (panels a and b)" and insert  
--Fig. 1A-1B--.

At page 6, line 15, please delete "Panel a" and insert --Fig 1A--.

At page 6, line 25, please delete "Panel b" and insert --Fig. 1B--.

At page 6, line 35, please delete "Fig. 2 (panels a and b)" and insert  
--Fig. 2A-2B--.

At page 6, line 39, please delete "Panel a" and insert --Fig 2A--.

At page 7, line 4, please delete "Panel b" and insert --Fig. 2B--.

At page 7, line 9, please delete "Fig. 3 (panels a and b)" and insert  
--Fig. 3A-3B--.

At page 7, line 11, please delete "Panel a" and insert --Fig 3A--.

At page 7, line 16, please delete "Panel b" and insert --Fig. 3B--.

At page 7, line 27, please delete "Fig. 4" and insert --Fig. 4A-4D--.

At page 7, line 28, please delete "Fig. 5" and insert --Fig. 5A-5D--.

At page 8, line 2, please delete "Fig. 9A-9C" and insert --Fig. 9A-9H--.

At page 8, line 4, please delete "Fig. 10A-10B" and insert --Fig. 10A-10F--.

At page 9, line 22, after "recipient of a", please delete "replicable" and insert  
--replicable--.

At page 9, line 33, after "A partial", please delete "promotor" and insert --promoter--.

At page 9, line 35, after "depend on the", please delete "bindiny" and insert --binding--.

At page 13, line 20, before "nuclear factor", please delete "endogeneous" and insert --endogenous--.

At page 17, line 19, after "DNA included", please delete "therebetween" and insert --there between--.

At page 18, line 37, after "expression of the", please delete "endogeneous" and insert --endogenous--.

At page 21, line 14, after "addition or", please delete "substraction" and insert --subtraction--.

At page 21, line 37, after "Alternatively, low", please delete "basel" and insert --basal--.

At page 22, line 20, after "the criteria", please delete "discussed" and insert --discussed--.

At page 23, line 8, after "the genetic", please delete "swith" and insert --switch--.

At page 25, line 26, after "virion protein 16.", please delete "Alternatively" and insert --Alternatively--.

At page 26, line 14, after "operably linked", please delete "promotor . The promotor may be an inducible promotor" and insert --promoter. The promoter may be an inducible promoter--.

At page 26, line 15, after "or a constitutive", please delete "promotor. Examples of such promotors" and insert --promoter. Examples of such promoters--.

At page 26, line 16, before "IE as taught by", please delete "promotor" and insert --promoter--.

At page 26, line 17, before "such as HSV-Tk", please delete "promotor" and insert --promoter--.

At page 26, line 29, after "promoters such as the", please delete "muring" and insert --murine--.

At page 26, line 36, after "control of", please delete "endogeneous" and insert --endogenous--.

At page 27, line 4, after "comprises a minimal", please delete "promotor" and insert --promoter--.

At page 27, line 19, after "the cytomegalovirus", please delete "promotor" and insert --promoter--.

At page 27, line 22, before "are employed as", please delete "promotor-enhancer" and insert --promoter-enhancer--.

At page 27, line 22, after "The", please delete "promotor" and insert --promoter--.

At page 27, line 38, after "linked to a minimal", please delete "promotor" and insert --promoter--.

At page 28, line 24, after "copies of the", please delete "microInjected" and insert --microinjected--.

At page 29, line 3, before "the chimeric embryo", please delete "implantating" and insert --implanting--.

At page 29, line 29, after "addition or", please delete "subtraction" and insert --subtraction--.

At page 30, line 12, after "culture is", please delete "continuosly" and insert --continuously--.

At page 30, line 28, before "reference herein", please delete "incorporatedas" and insert --incorporated as--.

At page 30, line 38, after "repeatedly a", please delete "chromosal" and insert

--chromosomal--.

At page 31, line 30, after "a minimal", please delete "promotor" and insert --promoter--.

At page 31, line 39, after "a minimal", please delete "promotor" and insert --promoter--.

At page 32, line 31, after "whereas", please delete "expresion" and insert --expression--.

At page 34, line 37, after "Tc (or ", please delete "analogue" and insert --analogue--.

At page 36, line 22, after "transient expression", please delete "experlments" and insert --experiments--.

At page 38, line 17, before "of the Xho I/Sal I", please delete "asymmetry" and insert --asymmetry--.

At page 41, line 18, after "increase in", please delete "luciferase" and insert --luciferase--.

At page 42, line 12, before "factors and/or RNA", please delete "transcription" and insert --transcription--.

At page 44, line 34, before "regulatory system", please delete "transcriptional" and insert --transcriptional--.

At page 70, line 11, before "operably linked", please delete "promotor" and insert --promoter--.

### In the claims

Please add new claims 18-22, as follows:

--18. A fusion protein which activates transcription comprising a first polypeptide which is a Tet repressor operatively linked to a second polypeptide which activates transcription in eukaryotic cells.

19. The protein of claim 18, wherein the Tet repressor is a Tn10-derived Tet repressor.
20. The protein of claim 18, wherein the second polypeptide comprises a transcription activation domain of herpes simplex virion protein 16.
21. The protein of claim 19, wherein the second polypeptide comprises the C-terminal 130 amino acids of herpes simplex virion protein 16.
22. The protein of claim 18, wherein the second polypeptide comprises a transcription activation domain selected from the group consisting of an acidic transcription activation domain, a proline-rich transcription activation domain, a serine/threonine-rich transcription activation domain and a glutamine-rich transcription activation domain.--

#### REMARKS

Claim 1 was originally filed in the application. New claims 18-22 have been added. Accordingly, claims 1 and 18-22 are pending.

The title has been amended to more accurately reflect the subject being claimed in the application. The specification also has been amended to correct a number of minor informalities. New claims 18-22 are directed to transcriptional activator fusion proteins. Support for these claims can be found in the specification at, for example, pages 24, line 22 through page 26, line 1 and in Example 1 (pages 41-49).

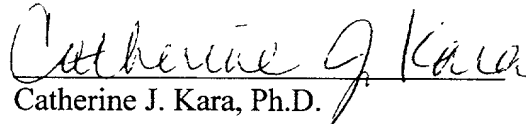
No new matter has been added by way of the amendments to the specification or the new claims. Applicants respectfully request that these amendments be entered.

#### SUMMARY

All pending claims are believed to be in condition for allowance. If a telephone conversation with Applicants' Agent would expedite the prosecution of the above-

identified application, the examiner is urged to call Applicants' Agent at (617) 227-7400.

Respectfully submitted,



Catherine J. Kara, Ph.D.

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Agent for Applicants

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Dated: September 29, 1998